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Short communication

Possibilities and challenges of "green" chromatographic solutions

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Introduction

In the last twenty years, the focus of the scientific community has been put on the "green" analytical chemistry (GAC). The concept of GAC includes development of new effective analytical methodologies that will enable minimization and / or elimination of the hazardous chemicals and chemical waste, but at the same time will enable faster and more energy efficient analysis (Guardia & Garrigues, 2020). Given that liquid chromatography (LC) is the most widely used analytical technique in the pharmaceutical analysis, as well as the large amount of chemical waste generated during these analyzes, the development of more environmentally friendly ("green") chromatographic methods is a crucial part of the GAC concept. Several approaches could be applied during the "green" chromatographic method development in order to remove / reduce the toxic organic solvents from the classical LC mobile phases (Napolitano-Tabares et al., 2021).

Considering that there is no entirely eco-friendly organic solvent, the use of pure water as a mobile phase appears to be an ideal solution. As the name of this technique implies, the “subcritical water chromatography” (SWH) uses pressurized hot water below its critical point conditions (374°C and 218 atm). This conditions require adaptation of the conventional LC instruments, such as heating system and detectors other than UV/Vis (e.g. amperometric detector, flame ionization detector) (Dembek & Bocian, 2020). However, this strategy for greening the chromatographic methods still has no wider application because it bears a certain financial burden for the analytical laboratories.

Another “green” solution is the use of columns packed with fully porous sub-2µm particles. This approach leads to faster chromatographic separation and reduction of the solvent consumption (Shaaban, 2016). However, this approach is not quite “green” because the consumption of the toxic solvents is not eliminated. In addition, the conventional LC instruments should be converted into UPLC systems, thus this expense is sometimes not acceptable for the laboratories with low-incomes.

In this review, the focus is given on the “green” chromatographic solutions that could be easily applied on the conventional LC instruments, without a need for further investements.

Eco-friendly solvents

The replacement of acetonitrile (ACN) and methanol (MeOH) used in the LC mobile phases with eco-friendlier ones, has a big role in the GAC strategies.

Ethanol (EtOH) is the first choice for “greening” the LC mobile phase. This solvent is an effective alternative for MeOH because they belong in the same group (according the Snyder’s classification of organic solvents); EtOH has higher elution power and low UV cutoff. The drawback of EtOH mobile phase is the higher column backpressure which could be overwhelmed with higher column temperatures or with the use of columns packed with superficially porous particles (Yabre, 2018).

2-propanol (IPA), acetone and ethyl acetate are greener alternatives for ACN, but the analysts should be aware of the higher viscosity of IPA and the high UV cutoff wavelength of acetone and ethyl acetate (330 nm and 260 nm, respectively) (Olives et al., 2017).

Propylene carbonate (PC) is another green polar aprotic solvent that has emerged as an alternative for ACN. The lower miscibility with water is overwhelmed with addition of EtOH, usually in ration 7/3 (*v/v*) (PC/EtOH or water/EtOH). These mixtures, compared to

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the previously mentioned solvents, have low UV cutoff (around 210 nm). The mass-transfer resistance and the higher backpressure of the PC/EtOH mobile phases could be overcome with lower flow rates (Tache, 2013).

Micellar liquid chromatography (MLC)

In the recent years, the increased awareness of the GAC principles contributed MLC to be back in the focus of the analysts (Kamal & El-Malla, 2019; Ibrahim et al., 2020). The greenness of this technique is seen through the aqueous composition of the mobile phase, low toxicity and cost, and low environmental impact of the surfactants. Namely, the mobile phase contains surfactant (usually sodium dodecyl sulfate) above its critical micellar concentration, while the separation is performed on the commonly used reverse-phase stationary phases (C_{18}, C_8).

The unique characteristics of the micellar mobile phase are responsible for the diverse interactions (hydrophobic, ionic and steric) between the analyte, the surfactant-modified stationary phase and the micelles. These interactions have impact on the retention and the selectivity, thus allowing separation of ionic and neutral compounds (Rambla-Alegre, 2012). The separation of hydrophobic compounds in MCL is a challenge because of the excessive retention. This drawback could be surpassed with the addition of small concentrations of Brij-35, which as a more polar non-ionic surfactant eliminates the need of the addition of low concentration of organic solvent (Ibrahim et al., 2020). In addition, shorter chain length stationary phases could be used. Considering the wide range of interactions and retention mechanisms in MCL, it is advisable to use the design of experiments approach for the optimization of the critical method parameters.

Per aqueous liquid chromatography (PALC)

Recent literature data (Bocian & Krzeminska, 2019; Dembek & Bocian, 2020) show that pure water on ambient temperature could be used as "green" chromatographic solutions for separation of polar compounds. The separation is performed on polar-embedded stationary phases using pure water or highly aqueous mobile phase. In PALC, the selectivity is controlled through the type of the stationary phase and the ionic strength and pH value of the aqueous buffer. Considering the differences in the solvation properties of the stationary phases, the right choice of the column type is crucial for the method performance.

Concluding remarks

Finding the ideal "green" solution for particular LC application is a challenge, but still there is enough scientific knowledge that could support this process. The analysts across the laboratories should more bravely implement the "green" chromatographic solutions. These "green" solutions bear benefits to the analyst (healthier and safer working environment); to the pharma industry (significant reduce of the waste disposal costs) and to the community (reduced negative environmental impact).

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